

HIGH THROUGHPUT GENERATION AND SCREENING OF FULLY HUMAN ANTIBODY REPERTOIRE IN YEAST

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ABSTRACT

Compositions, kits and methods are provided for generating highly
10 diverse libraries of proteins such as antibodies via homologous recombination
in vivo, and screening these libraries against protein, peptide and nucleic acid
targets using a two-hybrid method in yeast. The method for screening a library
of tester proteins against a target protein or peptide comprises: expressing a
library of tester proteins in yeast cells, each tester protein being a fusion
15 protein comprised of a first polypeptide subunit whose sequence varies within
the library, a second polypeptide subunit whose sequence varies within the
library independently of the first polypeptide, and a linker peptide which links
the first and second polypeptide subunits; expressing one or more target
fusion proteins in the yeast cells expressing the tester proteins, each of the
20 target fusion proteins comprising a target peptide or protein; and selecting
those yeast cells in which a reporter gene is expressed, the expression of the
reporter gene being activated by binding of the tester fusion protein to the
target fusion protein.

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